# Re-Evaluation of the FQPA Safety Factor for Pyrethroids

# Bottom Line

The FQPA safety factor has been reduced from 10X to 1X for pyrethroids based on a wealth of evidence, including available studies in the open literature, studies submitted to EPA for registration, over a decade of research specifically trying to address the FQPA safety factor, and recommendations from multiple science advisory panels (SAP).

# Background-2011 Decision

- In 2011, the FQPA safety factor was reduced from 10X to 3X, based on available information at the time
- Additional information on rats and humans was needed to conclude that there were no differences between children and adults (i.e. to reduce all the way to 1X)

# Available Information for the 2019 Reevaluation

- Published studies (>ten thousand citations reviewed)
- Studies submitted to EPA as part of registration/registration review
- Research conducted by CAPHRA (consortium of pyrethroid registrants)
  - CAPHRA was formed in 2011 with the aim of obtaining additional information to further refine the FQPA SF
  - Research mostly uses cells (instead of whole animals) and mathematical models known as PBPK models

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CAPHRA = Council for the Advancement of Pyrethroid Human Risk Assessment


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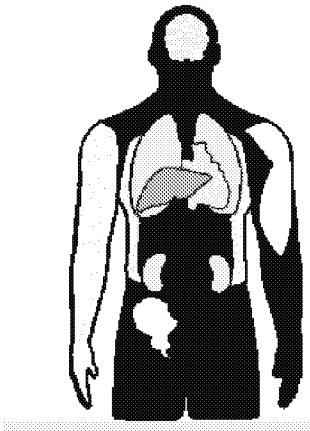
# How EPA Evaluated Available Information

- Comprehensive review of publicly available literature and studies submitted for pesticide registration
  - Incorporated information into individual pesticide assessments, when appropriate
- Extensive involvement on the pyrethroids by the public and scientific experts from outside the Agency
  - Multiple Science Advisory Panel (SAP) meetings (2007, 2009, 2010, and 2015)
  - Expert peer-review panel (2018)

# CAPHRA PBPK Model

- CAPHRA constructed mathematical models (known as physiologically based pharmacokinetic [PBPK] models) using rat and human tissues.
- Models were recommended by federal advisory groups and the National Academy of Sciences as a scientifically sound way to assess differences between children and adults
- Models specifically provide information for humans, which was not available at the time of the 2011 evaluation

# PBPK models predict chemical concentrations inside the body over time



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# Conclusions on FQPA SF

- PBPK models in 2019 support the conclusion that there are no differences between children and adults in humans following pyrethroid exposure
- The 10X FQPA SF can be reduced to 1X for all populations

# Conclusions on FQPA SF

- White paper with 2019 conclusions on FQPA SF published August 2nd, 2019.

https://www.epa.gov/ingredients-used-pesticide-products/2019-evaluation-fqpa-safety-factor-pyrethroids

- Paper is available for public comment with the pyrethroid preliminary interim decisions (PIDs) (released 11/12/19)

# CAPHRA models- Other uses

- CAPHRA models were specifically designed to address concerns regarding FQPA (i.e. potential differences between human juveniles and adults)
- Models are not ready to be used to address other uncertainty factors (additional data are needed)
- A second white paper is being drafted on this topic and will be released in the future

# Public Reception/Perception of the FQPA SF Decrease

- Some members of the public may distrust the data used to decrease the FQPA SF because part of these data were created by registrants
- Some NGOs such as the Center for Biological Diversity and the Environmental Working Group erroneously believe that any decrease in the FQPA SF means EPA is not protecting children

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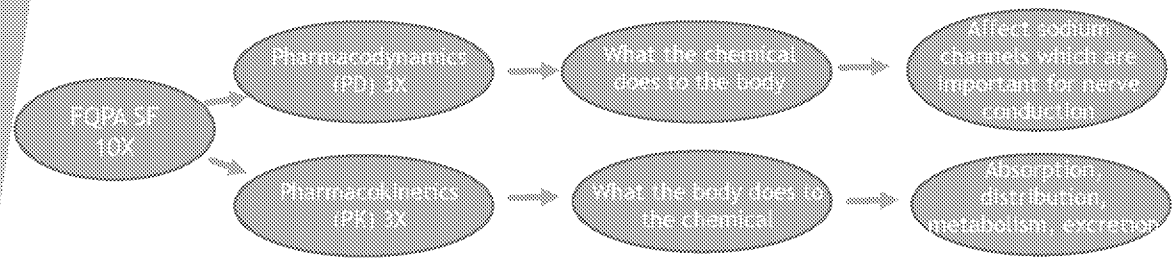
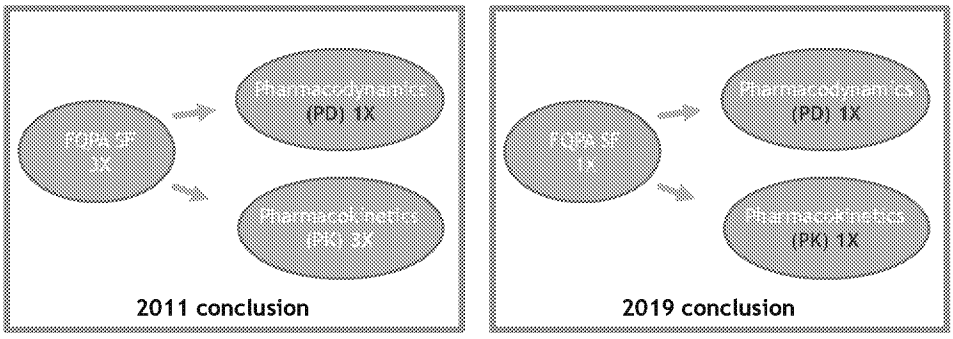
Additional slides- if needed

# FQPA Safety Factor

- FQPA default assumption → children/pregnant women up to 10X more sensitive than non-pregnant adults
- The 10X FQPA SF is retained unless there are reliable data to remove it



# Conclusions on FQPA SF




- Based on the 2019 analysis, the Agency concludes that the FQPA SF (PDxPK) can be reduced to 1X for all populations for the pyrethroid pesticides